

## CLAIM AMENDMENT AND LISTING

This listing of claims replaces all prior versions, and listings, of claims in this application.

Claim 1 (currently amended) A microfluidic device comprising:

- (a) a first elastomeric layer;
- (b) a second elastomeric layer on top of said first elastomeric layer, said second elastomeric layer comprising a pump and valve system for controlling the flow of fluid within said fluid flow channel, wherein said second elastic layer comprises a pressure channel;
- (c) a fluid flow channel within said elastomeric layer, said flow channel being about 500  $\mu\text{m}$  or less; and,
- (d) ~~a means for providing a fluid sample delivery device for delivering of~~ fluid from said ~~microfluidic device~~fluid flow channel to an analytical device~~mass spectrometer~~, said sample delivery device~~providing means~~ comprising a capillary having at least a portion thereof being located within said fluid flow channel ~~and being heretically sealed with said flow channel~~, said capillary being ~~[[ in]]~~ operatively interconnected to said analytical device~~mass spectrometer~~ for introducing said sample fluid from said fluid flow channel into said analytical device~~mass spectrometer~~ for analysis.

Claims 2-3 (canceled)

Claim 4 (original) The microfluidic device of Claim ~~[[3]]~~1, wherein said capillary forms a hermetic seal with said flow channel.

Claim 5 (canceled)

Claim 6 (original) The microfluidic device of Claim [[5]]1, wherein said analytical device is a selected from the group consisting of UV spectrometers, fluorescence spectrometers, IR spectrometers, gas chromatographic devices, liquid chromatographic devices, NMR devices, mass spectrometers and combinations thereof.

Claim 7 (original ) The microfluidic device of Claim 6, wherein said sample interface means comprises a means for generating a mist from the fluid flowing through said capillary, whereby said mist is introduced said analytical device for analysis.

Claim 8 (original) The microfluidic device of Claim 6, wherein said analytical device is a mass spectrometer.

Claim 9 (original) The microfluidic device of Claim 8, wherein said means for generating a mist comprises a device for applying electrospray voltage to said capillary to generate said mist.

Claim 10 (original) The microfluidic device of Claim 9, wherein the tip of said capillary comprising said sample interface means is tapered.

Claim 11 (canceled)

Claim 12 (canceled).

Claim 13 (canceled)

Claim 14 (currently amended) The microfluidic device of Claim 13, wherein said sample interface means comprises generating a mist using said pump and valve system.

Claim 15 (original) The microfluidic device of Claim 13 further comprising a sample preparation chamber within said fluid flow channel.

Claim 16 (original) The microfluidic device of Claim 15 wherein said sample preparation chamber comprises a rotary fluid flow channel and a means for circulating a fluid within said rotary fluid flow channel for conducting a chemical reaction, an assay, or other sample preparations within said rotary fluid flow channel.

Claim 17 (original) The microfluidic device of Claim 16, wherein said mean for circulating the fluid within said rotary fluid flow channel comprises said pump and valve system.

Claim 18 (currently amended) An analytical apparatus for analyzing a fluid sample comprising:

- (a) an analytical device for analyzing the fluid sample; and
- (b) a microfluidic device operatively interconnected to said analytical device, wherein said microfluidic device comprises a first elastic layer comprising a fluid flow channel and a means for introducing the fluid sample into said analytical device from said fluid flow channel,

wherein said microfluidic device further comprises a second elastic layer on top of said first elastic layer, said second elastic layer comprises a pressure channel for controlling the flow of fluid through said fluid flow channel, and said microfluidic device further comprises a pump and valve system within said second elastic layer for controlling the flow of fluid within said fluid flow channel.

Claim 19 (original) The analytical apparatus of Claim 18, wherein said analytical device is selected from the group consisting of UV spectrometers, fluorescence spectrometers, IR spectrometers, gas chromatography devices, LPLC devices, HPLC devices, NMR devices, mass spectrometers and combinations thereof.

Claim 20 (original) The analytical apparatus of Claim 19, wherein said analytical device is an electrospray ionization mass spectrometer or a nanoelectrospray mass spectrometer.

Claim 21 (original) The analytical apparatus of Claim 20, wherein said fluid sample introducing means comprises a means for generating an ionized mist from the fluid sample.

Claim 22 (original) The analytical apparatus of Claim 21, wherein said ionized mist generating means comprises a capillary having a distal end and a proximal end, wherein said proximal end of capillary is located within said fluid flow channel, and said distal end of capillary is interconnected to a device for applying electrospray voltage for generating the mist.

Claim 23 (original) The analytical apparatus of Claim 22, wherein the bore diameter of said distal end of capillary is about 100  $\mu\text{m}$  or less.

Claim 24 (original) The analytical apparatus of Claim 22, wherein said distal end of capillary is tapered.

Claim 25 (canceled)

Claim 26 (canceled)

Claim 27 (canceled)

Claim 28 (original) The analytical apparatus of Claim ~~[[27]]~~18 further comprising a sample preparation chamber within said fluid flow channel.

Claim 29 (original) The analytical apparatus of Claim 28, wherein said sample preparation chamber comprises a rotary fluid flow channel and a means for circulating a fluid within said rotary fluid flow channel for conducting a chemical reaction, an assay, or other sample preparations within said rotary fluid flow channel.

Claim 30 (original) The microfluidic device of Claim 29, wherein said mean for circulating the fluid within said rotary fluid flow channel comprises said pump and valve system.

Claim 31 (currently amended) A method for producing a microfluidic device comprising a means for introducing a fluid sample into an analytical device, said method comprising the steps of:

- (a) producing a first elastic layer of said microfluidic device, wherein said first elastic layer comprises a fluid flow channel; and
- (b) integrating a proximal end of a capillary within said fluid flow channel, wherein said step of integrating the capillary comprises the steps of:
  - (i.) producing a bottom portion of first elastic layer comprising a bottom portion of said fluid flow channel and a top portion of first elastic layer comprising a top portion of said fluid flow channel; and
  - (ii.) placing said proximal end of capillary in said bottom portion of said fluid flow channel on said bottom portion of first elastic layer and placing said top portion of first elastic layer on top of said first portion

of first elastic layer and forming a seal between said bottom and said top portions of first elastic layer to provide said first elastic layer comprising said fluid flow channel.

wherein a distal end of said capillary comprises said sample introducing means, and wherein said microfluidic device further comprises a second elastic layer on top of said first elastic layer, said second elastic layer comprises a pressure channel, said microfluidic device further comprises a pump and valve system within said second elastic layer for controlling the flow of fluid within said fluid flow channel.

Claim 32 (canceled)

Claim 33 (original) The method of Claim 32, wherein said first elastic layer is produced by a mixture of two polymer components.

Claim 34 (original) The method of Claim 33, wherein said bottom portion comprises an excess of one polymer component and said top portion comprises an excess of the other polymer component.

Claim 35 (original) The method of Claim 31, wherein said distal end of capillary is interconnected to a device for applying electrospray voltage for generating a mist for introducing the fluid sample into an electrospray ionization mass spectrometer or a nanoelectrospray mass spectrometer.

Claim 36 (original) The method of Claim 35, wherein said distal end of capillary is tapered.

Claim 37 (original) A method for analyzing a fluid sample using an analytical device comprising the steps of:

- (a) introducing said fluid sample into said analytical device through a fluid flow channel of a microfluidic device, wherein said fluid flow channel is located within a first elastic layer of said microfluidic device said microfluidic device further comprises a second elastic layer on top of said first elastic layer, said second elastic layer comprises a pressure channel, said microfluidic device further comprises a pump and valve system within said second elastic layer for controlling the flow of fluid within said fluid flow channel; and
- (b) analyzing said fluid sample using said analytical device.

Claim 38 (original) The method of Claim 37, wherein said microfluidic device further comprises a sample providing means interconnected to said fluid flow channel and a sample injection site of said analytical device for introducing said fluid sample into said analytical device from said fluid flow channel.

Claim 39 (original) The method of Claim 38, wherein said sample providing means comprises a capillary wherein a proximal end of said capillary is integrated with said fluid flow channel and the distal end of said capillary is operatively interconnected to said analytical device such that said fluid sample from said fluid flow channel is introduced into said sample injection site through said distal end of capillary.

Claim 40 (original) The method of Claim 39, wherein said analytical device is a selected from the group consisting of UV spectrometers, fluorescence spectrometers, IR spectrometers, gas chromatographic devices, liquid chromatographic devices, NMR devices, mass spectrometers and combinations thereof.

Claim 41 (original) The method of Claim 40, said analytical device is a mass spectrometer.

Claim 42 (original) The method of Claim 41, wherein said sample providing means comprises generating an ionized mist from said fluid sample.

Claim 43 (original) The method of Claim 42, wherein said ionized mist generating step comprises applying electrospray voltage to said distal end of capillary using an electrospray voltage device to generate said ionized mist.

Claim 44 (original) The method of Claim 43, wherein the tip of said distal end of capillary is tapered.

Claim 45 (original) The method of Claim 37, wherein said first elastic layer of microfluidic device further comprises a sample preparation chamber which is integrated with said fluid flow channel.

Claim 46 (canceled)

Claim 47 (canceled)

Claim 48 (canceled)

Claim 49 (currently amended) The method of Claim ~~[[48]]~~37, wherein said sample preparation chamber comprises a rotary fluid flow channel and a means for circulating a fluid within said rotary fluid flow channel.



Claim 50 (original) The method of Claim 49, wherein said mean for circulating the fluid within said rotary fluid flow channel comprises said pump and valve system.

Claim 51 (original) The method of Claim 50 further comprising the steps of preparing said fluid sample within said sample preparation chamber.

Claim 52 (original) The method of Claim 45, wherein said sample preparation step comprises conducting a sample preparation process within said sample preparation chamber, wherein said sample preparation process comprises:

- (i) conducting a chemical reaction;
- (ii) conducting an assay;
- (iii) degrading a peptide or protein;
- (iv) conducting a chemical analysis;
- (v) extraction of analytes from solvents;
- (vi) extraction of analytes from bodily fluids;
- (vii) concentration of sample analytes;
- (viii) affinity purification of an analyte;
- (ix) digesting a nucleic acid, carbohydrate, lipid or other molecule or mixture of molecules;
- (x) separation; and
- (xi) cell growth (mammalian, bacterial or parasite).

Claim 53 (original) The method of Claim 52, wherein said sample preparation step comprises conducting a combinatorial chemistry for preparation of an array of polymers from a monomer.

Claim 54 (original) The method of Claim 53, wherein said monomer is selected from the group consisting of nucleotides, amino acid peptides, carbohydrates, lipids, and precursors for combinatorial synthesis.

Claim 55 (original) The method of Claim 52, wherein said sample preparation step comprises conducting a receptor or an enzyme binding assay.

Claim 56 (original) The method of Claim 52, wherein said sample preparation step comprises conducting binding of a target molecule to an array of oligonucleotides, peptides, proteins, oligosaccharides, and small molecules.

Claim 57 (original) The method of Claim 52, wherein said sample preparation step comprises conducting an enzymatic degradation of proteins, peptides, oligonucleotides, carbohydrates, lipids, small molecules, or mixtures thereof.

Claim 58 (original) The method of Claim 45, wherein said microfluidic device comprises a plurality of sample preparation chamber.

Claim 59 (original) The method of Claim 58, wherein each fluid sample from said plurality of sample preparation chamber is independently analyzed by said analytical device.